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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/554,410	11/17/2005	Giovanni Paganelli	725.1049	4581

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EXAMINER	
GUSSOW, ANNE	
ART UNIT	PAPER NUMBER
1643	

NOTIFICATION DATE	DELIVERY MODE
12/08/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

info@lmiplaw.com

Office Action Summary	Application No.	Applicant(s)	
	10/554,410	PAGANELLI ET AL.	
	Examiner	Art Unit	
	Anne M. Gussow	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 November 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-7,9,11-14 and 18-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-7,9,11-14 and 18-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Upon further consideration by the examiner and in view of the NEW GROUNDS of Rejection below, the finality of the previous office action is withdrawn.

2. Claims 1, 3-7, 9, 11-14, 18-22, 24-29, and 31-39 have been amended.
Claims 2, 8, 10, and 15-17 have been cancelled.

3. Claims 1, 3-7, 9, 11-14, and 18-39 are under examination.

4. The following office action contains NEW GROUNDS of Rejection.

Rejections Withdrawn

5. The rejection of claims 1, 3-7, 9, 11-13, 18-29, and 30-39 under 35 U.S.C. 103(a) as being obvious over Goldenberg in view of Cokgor, et al. is withdrawn in view of applicant's arguments and the new grounds of rejection below.

6. The rejection of claims 1, 3-7, 11-14, 18-29, and 30-39 under 35 U.S.C. 103(a) as being obvious over Goldenberg in view of Cokgor, et al. and MacPhee, et al. is withdrawn in view of applicant's arguments and the new grounds of rejection below.

NEW GROUNDS of Rejection

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1, 3-7, 9, 11-14, 18-39 rejected under 35 U.S.C. 103(a) as being unpatentable over Rusckowski, et al. (Journal of Nuclear Medicine, 1996. Vol. 37, pages 1655-1662) or Samuel, et al. (Journal of Nuclear Medicine, 1996. Vol. 37, pages 55-61) in view of Goldenberg (US PG PUB 2001/0006618, published July 5, 2001, as cited on the PTO-892 mailed November 26, 2007), Cokgor, et al. (Journal of Clinical Oncology, 2000. Vol. 18, pages 3862-3872, as cited on the PTO-892 mailed November 26, 2007) and MacPhee, et al. (US PAT 6,054,122, issued April 25, 2000, as cited on the PTO-892 mailed January 5, 2009).

The claims recite a method of treating a patient with a solid tumor, said method comprising: (a) administering intraoperatively via a locoregional route to said patient a first agent endowed with tumor tropism, wherein said first agent is selected from the group consisting of avidin, streptavidin, their polymeric derivatives and their derivatives with polyethyliene glycol capable of concentrating locally on the tumor or in the vicinity of it and then (b) administering postoperatively via a systemic route a second anticancer agent with affinity for said first agent, whereby increased accumulation of said first agent endowed with tumor tropism reduces the amount of said second anticancer agent to be administered, wherein said first agent is avidin, wherein said first agent is avidin and said second anticancer agent is a biotinylated anticancer agent, wherein said second anticancer agent comprises an anticancer agent selected from the group consisting of radioisotopes, chemotherapeutic agents, toxins and anticancer agents, wherein said anticancer agent is a radioisotope selected from the group consisting of Fe-52, Mn-52m, Co-55, Cu-64, Ga-67, Ga-68, Tc-99, In-111, 1-123, 1-125, 1-131, P-32, Sc-47, Cu-67,

Y-90, Pd-109, Ag- 111, 1-131, Pro-149, Re-186, Re-188, At-211, Pb-212, Bi-212 and Lu-177, wherein said solid tumor is selected from the group consisting of breast, pancreas, lung, pleural, peritoneal, cervico-facial, brain and bladder tumors, wherein said first agent and second anticancer agent are administered by injection, wherein said first agent is successively administered by syringe in precise volume, in which wherein said first agent is administered in a single dose, wherein said first agent is administered by spray or by injection in the tumor bed and surrounding tissue.

Rusckowski, et al. teach administration of unlabeled streptavidin followed by radiolabeled biotin for the detection of osteomyelitis.

Samuel, et al. teach administration of nonspecific avidin followed by radiolabeled biotin for the detection of vascular graft infection. Rusckowski, et al. and Samuel, et al. do not teach treatment of tumor by administering avidin. Rusckowski, et al. and Samuel, et al. do not teach locoregional administration of the first agent by a spray. These deficiencies are made up for in the teachings of Goldenberg, Cokgor, et al. and MacPhee, et al.

Goldenberg teaches a method for treating tumor by injecting a patient with a first agent comprising an avidin- or biotin-conjugated antibody which binds to a marker produced by or associated with the lesion and a second agent comprising either avidin or biotin and a radiolabel (paragraphs 36 and 61). Goldenberg teaches suitable radiolabels to include Yittruim-90 (paragraph 114). Goldenberg teaches dosing the first and second agents 24 hours apart (paragraph 133). Goldenberg teaches the method can be used for treating ovarian tumors (example 3).

Cokgor, et al teach administration of radiolabeled 81C6 antibody directly to the surgical resection cavity in patients with malignant gliomas.

MacPhee, et al. teach administration of supplemented tissue sealant (TS) by spraying (column 25 lines 27-44). The TS may be supplemented with growth factors, drugs or antibodies (column 12 lines 19-53).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the unlabeled streptavidin of Rusckowski, et al. or the nonspecific avidin of Samuel, et al. to target the cancer in the treatment method of Goldenberg in the administration method as taught by Cokgor, et al. and the spray administration as taught by MacPhee, et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have used the unlabeled streptavidin of Rusckowski, et al. or the nonspecific avidin of Samuel, et al. to target the cancer in the treatment method of Goldenberg in the administration method as taught by Cokgor, et al. and the spray administration as taught by MacPhee, et al. because both Rusckowski, et al. and Samuel, et al. teach localization of the avidin compound to the area of interest despite systemic administration of the avidin. Additionally, Goldenberg, et al. teach administration of avidin/biotin compounds for the treatment of tumors. Therefore, one of ordinary skill in the art would have expected the unlabeled avidin compound to target to the tumor tissue in the surgical cavity. Further, Cokgor, et al. teach that systemically administered antibodies are not as effective in the treatment of brain tumors because antibodies do not cross the blood brain barrier well and there is high interstitial fluid

pressure in the tumor and surrounding normal tissue, providing support for localized administration of the avidin compounds. Thus, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the agent of Goldenberg in the administration method of Cokgor, et al.

Applicant's arguments regarding the Goldenberg reference have been considered by the examiner. The examiner agrees that Goldenberg teaches administration of a conjugated avidin molecule. However, the Rusckowski and Samuel references support administration of unlabeled and nonspecific avidin for localization to a diseased site, therefore the method of Goldenberg would not be limited to labeled or conjugated avidin molecules.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

11. No claims are allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne M. Gussow whose telephone number is (571)272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anne M. Gussow
December 4, 2009

/Anne M. Gussow/
Examiner, Art Unit 1643